IN THE DRAWINGS

Substitute drawings are enclosed herewith.

REMARKS

This responds to the Office Action mailed on April 22, 2009.

Claims 1-4, 6-8, 10, 13, and 35 are amended, and claims 173-174 are added. Claims 1-4, 6-11, 13, 27-37, and 168-174 are pending.

Substitute drawings which address the objections thereto are enclosed herewith.

Claims 168-172 were objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. However, claim 1, on which claims 168-172 depend, is directed to a method comprising (open ended language) contacting a sample with a substrate having wild-type and mutant mecA capture oligonucleotides, while claims 168-172 specify that the substrate may also include other non-mecA capture oligonucleotides. Thus, claims 168-172 are in compliance with 37 C.F.R. § 1.75(c).

The 35 U.S.C. § 112, First Paragraph, Rejection

Claims 1-4, 6-8, 10, 13, 27-37, and 168-172 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement because the quantity of experimentation to enable the full scope of the claimed invention is allegedly great with little if any reasonable expectation of success. This rejection, as it may be maintained with respect to the pending claims, is respectfully traversed.

Under the section entitled "The amount of direction or guidance presented/the presence or absence of working examples" (pages 6-7 of the Office Action), the Examiner asserts that Applicant was only able to obtain a detectable result when a specific signal amplification step (silver staining) was performed because the specification at page 58 discloses "the attached nanoparticles could not be visualized with the naked eye. In order to facilitate the visualization …a signal amplification method…was employed.". The Examiner continues, asserting that a review of the disclosure fails to find where Applicant contemplated alternative test conditions.

However, the Examiner appears not to have considered that the cited portion of the specification states that "[a]t the target amounts tested (250 ng (7.5 E7 copies) - 1 μg (3.0 E8), the attached nanoparticles could not be visualized with the naked eye" (emphasis added). That statement does not support a conclusion that the method can only be practiced with a signal amplification step. As previously pointed out in the Amendment filed on February 13, 2009, the specification discloses other methods to detect the nanoparticles that do not employ silver staining (see, e.g., claims 13, 28-29 and 35 and pages 29-31 of the specification). The Examiner failed to specifically address that evidence (that other detection methods are disclosed in the specification) in the Office Action, as required by M.P.E.P. § 2164.05. Based on that, it is Applicant's position that the finality of the Office Action should be withdrawn.

Further evidence that gold nanoparticles may be detected by means other than silver enhancement is provided in the following abstracts: Elghanian et al. (*Science*, 277:1078 (1997), "Selective colorimeteric detection of polynucleotides based on the distance-dependent optical properties of gold nanoparticles"); Solokov et al. (*Cancer Res.*, 63:1999 (2003), "Real-time vital optical imaging of precancer using anti-epidermal growth factor receptor antibodies conjugated to gold nanoparticles"); and Park et al. (*Science*, 295:1447 (2002), "Array-based electrical detection of DNA with nanoparticle probes") (a copy of each is enclosed herewith).

Therefore, it was well within the skill of the art, as of Applicant's filing date, to detect gold nanoparticles by a variety of methods.

Under the section entitled "The state of the prior art/the predictability or unpredictability of the art" (pages 8-10 of the Office Action), the Examiner cites page 14 of Zhang et al. (*Bioinformatics*, volume 19 (2003)); paragraph 0018 in Chan (U.S. Publication No. 2002/0119455); paragraph 0036 in Barany et al. (U.S. Publication No. 2007/0042419); paragraph 0035 in Choi et al. (U.S. Publication No. 2007/0042400); paragraph 0037 in Yasuno et al. (U.S. Publication No. 2007/0031829); paragraph 0004 in Wang et al. (U.S. Publication No. 2007/0009954); paragraph 0004 in Rowlen et al. (U.S. Publication No. 2006/0286570); and column 40 of Jones (U.S. Patent No. 5,858,671).

It is unclear to Applicant how the cited portions of Zhang et al. and Chan, related to errors in DNA sequencing by hybridization, and Jones, related to synthesizing oligonucleotides for arrays (note that Jones has an effective filing date of 1996 and so is clearly not "state of the

art"), are pertinent to Applicant's method, which is not directed to DNA sequencing or synthesizing oligonucleotides for arrays.

And with regard to the "difficulty" or expense in developing or performing assays to detect mutant DNA such as DNA with a single point mutation (Barany et al., Choi et al., Yasuno et al., Wang et al., and Rowlen et al.), it is clearly within the skill of the art to develop and perform such as assays, as evidenced by paragraph 0004 in Wang et al. ("[a] number of methods have been developed to score SNPs, including allele-specific hybridization, electrophoretic DNA sequencing, single-nucleotide extension using labeled chain terminators, the 'Invader' assay…" Moreover, the expense of development or in performing an assay is not relevant to the enablement inquiry. The Examiner is reminded that the test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the specification coupled with information known in the art without undue experimentation. M.P.E.P. § 2164.01 (citing United States v. Telectronics, Inc., 857 F.2d 778, 785, 8 U.S.P.Q.2d 1217, 1223 (Fed. Cir. 1988)).

Additional evidence that, as of Applicant's filing date, it was within the skill of the art to detect single nucleotide polymorphisms is provided by the following abstracts: Tolley et al. (*Anal. Biochem.*, 315:223 (2003), "Single-chain polymorphism analysis in long QT syndrome using planar waveguide fluorescent biosensors"); Marques et al. (*Clin. Chem. Lab. Med.*, 41:475 (2003), "Electrochemical DNA sensor for detection of single nucleotide polymorphisms"); Gerion et al. (*Anal. Chem.*, 75:4766 (2002), "Room-temperature single-nucleotide polymorphism and multiallele DNA detection using fluorescent nanocrystals and microarrays"); and Maxwell et al. (*J. Am. Chem. Soc.*, 124:9606 (2002), "Self-assembled nanoparticle probes for recognition and detection of biomolecules") (a copy of each is enclosed herewith).

At page 10 of the Office Action, the Examiner asserts that the claimed method places no lower limit on the ability to accurately and reproducibly detect binding.

It is not the function of the claims to exclude all possibly inoperable embodiments. In re Anderson, 471 F.2d 1237, 176 U.S.P.Q. 331 (C.C.P.A. 1973); Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 224 U.S.P.Q. 409 (Fed. Cir. 1984); In re Dinh-Nguyen, 181 U.S.P.Q. 46 (C.C.P.A. 1974). Nevertheless, the claims recite that the conditions are effective for hybridization of the capture oligonucleotides to the first portion of the mecA gene sequence,

hybridization of the probe to the second portion of the mecA gene sequence, and discrimination between the wild-type mecA gene sequence and the mutant mecA gene sequence, and that detection of the gold nanoparticle at an address on the substrate having the one or more mutant capture oligonucleotides contacted with the sample is indicative that the sample has genomic DNA from an antibiotic resistant *Staphylococcus* bacteria.

At page 11 of the Office Action, the Examiner alleges that the specification does not provide the starting materials whereby any species of plant, virus, microbe or animal can be identified and that the claims do not distinguish between the size of the nanoparticles, the length composition and linking aspects of the probe to the nanoparticle, and the chemical formulation of the nanoparticle.

The Examiner is respectfully reminded that Applicant need not teach what is well known to the art. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81, 94-95 (Fed. Cir. 1986). It is Applicant's position that it is well within the skill in the art to prepare and use oligonucleotide-nanoparticle conjugates (see, for instance, U.S. Patent Nos. 6,361,944, 6,417,340, and 6,506,564, and PCT/US02/16382 and PCT/US03/14100, cited at page 27 of the specification, as well as the abstracts for Elghanian et al., Solokov et al. and Park et al., *supra*).

Example 4 in the specification discloses a hybridization based method to distinguish between *Staphylococcus* having wild-type and/or mutant *mec*A genes. Thus, it is Applicant's specification, in view of the skill of the art worker, that provides the requisite degree of predictability for the claimed method.

With regard to melting properties of nanoparticle-oligonucleotide conjugates, the Examiner is requested to consider Sun et al. (*Physica A,* 350:89 (2005)) (copy enclosed) and U.S. Patent No. 6,750,016.

As the specification provides adequate guidance to one of skill in the art, Applicant's specification is enabling.

Therefore, withdrawal of the § 112, first paragraph, enablement rejection is respectfully requested.

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CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's representative to facilitate prosecution of this application.

Respectfully submitted,

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